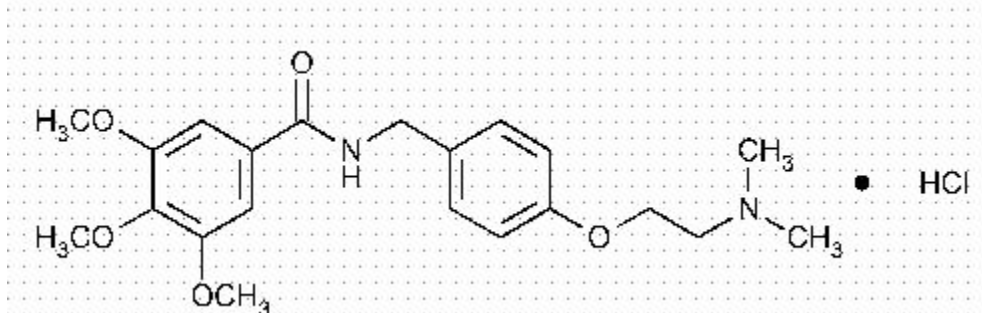


TRIMETHOBENZAMIDE HYDROCHLORIDE - trimethobenzamide hydrochloride capsule

Actavis Totowa LLC

DESCRIPTION

Chemically, trimethobenzamide hydrochloride is N-[p-[2-(dimethylamino)ethoxy]benzyl]-3,4,5-trimethoxybenzamide monohydrochloride. It has a molecular weight of 424.92 and the following structural formula:



Each capsule for oral use contains trimethobenzamide hydrochloride equivalent to 300 mg.

Inactive Ingredients: Lactose monohydrate, magnesium stearate and pregelatinized starch. The capsule shell contains the following ingredients, D&C Red #28, FD&C Blue #1, FD&C Red #40, gelatin and titanium dioxide.

White ink contains the following ingredients: ammonium hydroxide, isopropyl alcohol, n-butyl alcohol, pharmaceutical glaze, propylene glycol, simethicone and titanium dioxide.

CLINICAL PHARMACOLOGY

Mechanism of Action

The mechanism of action of trimethobenzamide hydrochloride as determined in animals is obscure, but may involve the chemoreceptor trigger zone (CTZ), an area in the medulla oblongata through which emetic impulses are conveyed to the vomiting center; direct impulses to the vomiting center apparently are not similarly inhibited. In dogs pretreated with trimethobenzamide hydrochloride, the emetic response to apomorphine is inhibited, while little or no protection is afforded against emesis induced by intragastric copper sulfate.

Pharmacokinetics

The pharmacokinetics of trimethobenzamide have been studied in healthy adult subjects. Following administration of 200 mg (100 mg/mL) trimethobenzamide I.M. injection, the time to reach maximum plasma concentration (T_{max}) was about half an hour, about 15 minutes longer for trimethobenzamide 300 mg oral capsule than an I.M. injection. A single dose of trimethobenzamide 300 mg oral capsule provided a plasma concentration profile of trimethobenzamide similar to trimethobenzamide 200 mg I.M. The relative bioavailability of the capsule formulation compared to the solution is 100%. The mean elimination half-life of trimethobenzamide is 7 to 9 hours.

Special Populations

Gender

Systemic exposure to trimethobenzamide was similar between men (N=40) and women (N=28).

Race

Pharmacokinetics appeared to be similar for Caucasians (N=53) and African Americans (N=12).

INDICATIONS AND USAGE

Trimethobenzamide hydrochloride capsule, USP 300 mg is indicated for the treatment of postoperative nausea and vomiting and for nausea associated with gastroenteritis.

CONTRAINDICATIONS

Use in patients with known hypersensitivity to trimethobenzamide is contraindicated.

WARNINGS

Caution should be exercised when administering trimethobenzamide hydrochloride capsules to children for the treatment of vomiting. Antiemetics are not recommended for treatment of uncomplicated vomiting in children and their use should be limited to prolonged vomiting of known etiology. There are two principal reasons for caution:

1. The extrapyramidal symptoms which can occur secondary to trimethobenzamide hydrochloride capsules may be confused with the central nervous system signs of an undiagnosed primary disease responsible for the vomiting, e.g., Reye's syndrome or other encephalopathy.
2. It has been suspected that drugs with hepatotoxic potential, such as trimethobenzamide hydrochloride capsules, may unfavorably alter the course of Reye's syndrome. Such drugs should therefore be avoided in children whose signs and symptoms (vomiting) could represent Reye's syndrome.

Trimethobenzamide hydrochloride capsules may produce drowsiness. Patients should not operate motor vehicles or other dangerous machinery until their individual responses have been determined.

Usage in Pregnancy:

Trimethobenzamide hydrochloride was studied in reproduction experiments in rats and rabbits and no teratogenicity was suggested. The only effects observed were an increased percentage of embryonic resorptions or stillborn pups in rats administered 20 mg and 100 mg/kg and increased resorptions in rabbits receiving 100 mg/kg. In each study these adverse effects were attributed to one or two dams. The relevance to humans is not known. Since there is no adequate experience in pregnant or lactating women who have received this drug, safety in pregnancy or in nursing mothers has not been established.

Usage with Alcohol: Concomitant use of alcohol with trimethobenzamide hydrochloride capsules, USP 300 mg may result in an adverse drug interaction.

PRECAUTIONS

During the course of acute febrile illness, encephalitis, gastroenteritis, dehydration and electrolyte imbalance, especially in children and the elderly or debilitated, CNS reactions such as opisthotonos, convulsions, coma and extrapyramidal symptoms have been reported with and without use of trimethobenzamide hydrochloride capsules or other antiemetic agents. In such disorders caution should be exercised in administering trimethobenzamide hydrochloride capsules, particularly to patients who have recently received other CNS acting agents (phenothiazines, barbiturates, belladonna derivatives). Primary emphasis should be directed toward the restoration of body fluids and electrolyte balance, the relief of fever and relief of the causative disease process. Overhydration should be avoided since it may result in cerebral edema.

The antiemetic effects of trimethobenzamide hydrochloride capsules may render diagnosis more difficult in such conditions as appendicitis and obscure signs of toxicity due to over dosage of other drugs.

ADVERSE REACTIONS

There have been reports of hypersensitivity reactions and Parkinson-like symptoms. There have been instances of hypotension reported following parenteral administration to surgical patients. There have been reports of blood dyscrasias, blurring of vision, coma, convulsions, depression of mood, diarrhea, disorientation, dizziness, drowsiness, headache, jaundice, muscle cramps and opisthotonos. If these occur, the administration of the drug should be discontinued. Allergic-type skin reactions have been observed; therefore, the drug should be discontinued at the first sign of sensitization. While these symptoms will usually disappear spontaneously, symptomatic treatment may be indicated in some cases.

DOSAGE AND ADMINISTRATION

(See WARNINGS and PRECAUTIONS.)

Dosage should be adjusted according to the indication for therapy, severity of symptoms and the response of the patient.

Usual Adult Dosage: One 300 mg capsule t.i.d. or q.i.d.

HOW SUPPLIED

Trimethobenzamide hydrochloride capsules, USP 300 mg are filled gelatin capsules size 1 lavender opaque cap/lavender opaque body with a white imprint "A-185" on cap and body. Available in bottles of 100's and 500's.

Store at 20° to 25°C (68° to 77°F)[See USP Controlled Room Temperature].



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